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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	**PAPER NUMBER**
1657	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/518,987	SIX ET AL.	
	Examiner	Art Unit	
	Satyendra K. Singh	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6 and 9-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6 and 9-29* is/are rejected.

7)☒ Claim(s) *17-21 and 23-29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 24th 2007 has been entered.

Claims 3, 7 and 8 have been cancelled by applicant's amendments to the claims.

Claims 1, 2, 4-6, 9-15 and newly added claims 16-29 have been entered, and are examined on their merits in this office action.

Election/Restrictions

The election of species (as previously set forth by the examiner and elected by applicants as Eudragit E100) has been **withdrawn** and all the species have been rejoined and examined for their patentability in this office action.

Claim Objections

1. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for **failing to further limit** the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The newly added claim 18 recites "The solid dispersion according to claim 1 wherein the polymer allowing a homogenous dispersion is a copolymer of vinylpyrrolidone and vinylacetate." And therefore, fails to further limit the limitation of the first polymer as recited in claim 1. Appropriate correction is required.

2. Claims 17, 19-21 and 23-29 (newly added) are objected to under 37 CFR 1.75 as being a **substantial duplicates** of claims 2, 4-6, and 9-15. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Appropriate correction is required.

3. Claim 4 is objected to under 37 CFR 1.75 as being a **substantial duplicates** of claim 6 (as they depends from claim 1, as currently amended). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Appropriate correction is required.

4. Claims 19 and 20 (newly added) are objected to under 37 CFR 1.75 as being a **substantial duplicates** of claims 21 and 22, respectively (as they depend from claim 1, as currently amended). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1 and 16 (as currently amended) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains **subject matter which was not described** in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 16 (newly added) recite the limitation "wherein said first polymer and said second polymer are present in a ratio of **about** 70:30 to **about** 80:20" (see instant claim 1), and "wherein said first polymer and said second polymer are present in a ratio of **about** 70:30"(see instant claim 16). The disclosure provided by applicants in the original claim 7 ("wherein a Eudragit E100/PVPVA 64 ration varies between 70/30 and 80/20"; see also figures 12 and 13, in particular), does not provide an explicit support for the claimed invention as currently presented by applicants. In addition, applicants in their response filed with the office have not pointed to a proper support for such amendments to the claim 1. In addition, such a ratio for the solid dispersion as claimed in instant claims 1 and 16 (i.e. Hydroxy-propyl methylcellulose and a copolymer of vinylpyrrolidone and vinylacetate, in combination) is not disclosed and supported by the instant disclosure provided by applicants.

Since, the claimed invention is not fully supported by the instant disclosure, either in the narrative or generic or in the examples or in the original claims provided by applicants, the claimed limitation constitutes **a new matter** situation. Appropriate explanation/correction is required.

Response to Applicant's Arguments

Applicant's arguments regarding the 112-first paragraph rejection of record (see response, page 6, in particular) for insertion of new matter in the form of limitation "**about** 70:30 to **about** 80:20" over claim 1 is fully considered but is not found to be persuasive because the arguments presented by the counsel do not seem to pertain to the situation in hand. As discussed in the above rejection, the limitations as recited in claim 1 (and newly added claim 16, as currently amended) are not supported in the original disclosure, drawing and claims, as filed by the applicants. Moreover, applicant's disclosure is suggestive of the fact that the dissolution rate critically depends on the particular ratio of the polymeric matrices used and therefore, does not seem to have room for variations outside the two ranges (such as "**about** 70:30 to **about** 80:20) as implied by applicants (i.e. implicit support) in their arguments (see instant disclosure figures 12-13, in particular).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1 and 16 (as currently amended) are rejected under 35 U.S.C. 112, second paragraph, as being **indefinite** for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 16 recite the limitations "ratio of about **70:30** to about **80:20**" and "ratio of about **70:30**", respectively, which is confusing. It is not clear as to what exactly is encompassed by the limitations as presented by applicants. It is unclear if said ratio or range of ratio for

said first and said second polymer refers to their respective amounts by weight or volume, or a combination thereof, or by any other standard implied therein (especially when the identity of the second polymer is not clear from the recited claims). The instant disclosure, as originally filed by the applicants, fails to provide any such guidance pertaining to the ratio of said polymers used in the invention as claimed. Appropriate explanation/correction is required.

2. Claims 2 and 17 rejected under 35 U.S.C. 112, second paragraph, as being **indefinite** for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims recite limitation "**stabilizing effect**", which is confusing. It is not clear as to what exactly is encompassed by the limitation presented in the claim especially, in the absence of any relevant guidance or definition for the term (pertaining to the kind or degree of stabilization) provided in the original disclosure by applicants. In addition, it is not clear if such an "stabilizing effect is imparted through a third polymer (?) or through the polymers (i.e. "first" and "second" polymers) already present in the invention as claimed (see claim 1, and claim 16, in particular). Appropriate explanation/correction is required.

3. Claims 9 and 23 recite the limitation "**the bioavailability**". There is insufficient **antecedent basis** for this limitation in the claim 1 (from which claims 9 and 23 depend from). Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1, 2, 4-6 and 9-29 (as currently amended) are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenberg et al (WO 02/11694 A2; IDS) in view of Baert et al (WO 97/44014; IDS) or Jung et al (WO 99/33467; IDS).

Claims are generally drawn to a solid dispersion comprising a poorly soluble bioactive compound dispersed in a polymeric matrix that comprises a first polymer that allows a homogeneous or molecular dispersion of the bioactive compound in the polymer matrix (such as a copolymer of vinylpyrrolidone and vinylacetate), and a second polymer that has a dissolution profile associated with the creation of a micro-environment enhancing the dissolution of the bioactive compound in an aqueous environment (such as hydroxyl-propyl methylcellulose or a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters), wherein said first polymer and said second polymer are present in a ratio of about 70:30, or in a ratio of about 70:30 to about 80:20 (see amended claims 1 and 16, in particular).

Rosenberg et al (IDS) teach antifungal compositions and dosage forms (such as solid dispersions suitable for application in the oral cavity) comprising a poorly bioavailable pharmaceutical active ingredient (such as itraconazole; see Rosenberg et al, abstract, page 2, lines 10-43, and claims, in particular) dispersed in a pharmaceutically acceptable matrix that can comprise of polymers such as hydroxyalkyl

alkylcellulose (i.e. HPMC, hydroxyl-propyl methylcellulose), or Eudragit ™ (i.e. a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters), or homo- and copolymers of n-vinylpyrrolidone/vinyl acetate (similar to the polymeric matrix, PVPVA 64 or a copolymer of vinylpyrrolidone and vinylacetate, as claimed; see Rosenberg et al, page 3, lines 6-17, in particular). Rosenberg et al teach the solid dispersions comprising a class II drug, itraconazole and a combination of polymer matrices such as n-vinylpyrrolidone/vinyl acetate copolymer and hydroxypropyl cellulose (HPC) that provide homogeneous dispersion and enhanced solubility under aqueous conditions of the oral cavity (see Rosenberg et al, page 7, examples 1-3; page 6, lines 14-24, in particular).

However, although suggested by the prior art (see Rosenberg et al, discussion supra), solid dispersions comprising a poorly soluble bioactive compound dispersed in a combination of polymer matrices as claimed in instant claims 4, 6, 19 and 21 (i.e. a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters or Eudragit E100, and a copolymer of vinylpyrrolidone and vinylacetate or PVPVA64), or claims 5, 20 and 22 (i.e. **HPMC** and a copolymer of vinylpyrrolidone and vinylacetate) are not explicitly taught by the referenced invention of Rosenberg et al.

Baert et al (IDS) teach antifungal compositions in the form of solid dispersions having improved bioavailability in an aqueous environment such as gastric fluid (see Baert et al, abstract, page 12-13, examples 1-5, and claims, in particular), wherein the polymer matrix comprises a polymer having a stabilizing effect on the bioactive compound (such as antifungal drug, itraconazole) in solution (see page 4, 2nd

paragraph, in particular), wherein the polymer allowing enhanced dissolution of the bioactive compound in an aqueous environment is hydroxypropyl methylcellulose (see Baert et al, page 12, in particular), wherein the polymer allowing a homogeneous dispersion is crospovidone (a crosslinked polyvinylpyrrolidone, PVP, i.e. a derivative of PVP, functional equivalent to a copolymer of vinylpyrrolidone and vinylacetate or PVPVA64 as claimed in the instant invention; see Baert et al, page 10, 3rd and last paragraph, in particular), wherein one or more polymer matrices comprise HPMC and crospovidone. The limitations of claims 9, 10, 23 and 24 are disclosed by the referenced invention as Baert et al teach solid dispersions comprising polymer matrix that enhance bioavailability of an orally administered bioactive compound, such as a class II drug (see the disclosure provided by the applicants, page 3, lines 16-18 of the instant specification), itraconazole/saperconazole (see Baert et al, page 10, in particular). The limitations of instant claims 14,15, 28 and 29 (wherein the solid dispersions are prepared by extrusion or spray drying processes; product by process claims) are also met by the solid dispersions comprising itraconazole and polymer matrices such as HPMC and crospovidone (see Baert, discussion supra) that provide enhanced bioavailability to the antifungal drug when ingested orally. Thus the teachings of Baert et al, as discussed supra, disclose a solid dispersion comprising a bioactive, antifungal compound, itraconazole and HPMC (hydroxypropyl methylcellulose) in combination with crospovidone (a crosslinked polymer of polyvinylpyrrolidone, i.e. a functional equivalent) that are suitable for enteric compositions that are administered orally.

Jung et al (IDS) teach method and composition (solid dispersions) of an oral preparation of itraconazole comprising aminoalkyl methacrylate copolymer (i.e. Eudragit E; see abstract, examples 1-7, tables 3-5, and claims, in particular) that is suitable for oral ingestion and antifungal treatment. Jung et al also suggest the use of other polymer matrices in combination with Eudragit, such as crospovidone (as diluent; see Jung et al, page 8, 3rd paragraph, in particular).

It would have been obvious to a person of ordinary skill in the art at the time this invention was made to modify the composition (i.e. solid dispersions) taught by Rosenberg et al such that the solid dispersions comprise of the poorly bioactive compound in two different polymeric matrices in combination with n-vinylpyrrolidone/vinyl acetate copolymer, such as HPMC or Eudragit (i.e. a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters), as explicitly suggested by the disclosures of Baert et al or Jung et al.

One of ordinary skill in the art would have been motivated at the time of invention to make such substitutions in the composition or solid dispersions of Rosenberg et al (i.e. using HPMC, or a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters such as Eudragit E as polymer matrices) in order to obtain resulting composition comprising a bioactive agent of class II or class IV (in combination, such as itraconazole dispersed in a polymer matrix such as a copolymer of polyvinylpyrrolidone) as suggested by the references (Baert et al, or Jung et al) with a reasonable expectation of success. The claimed subject matter fails to patentably

distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

The limitation "wherein said first polymer and said second polymer are present in a ratio of **about 70:30 to about 80:20** (or in a ratio of about 70:30, as recited in newly added claim 16), would have been a matter of routine optimization to a person of ordinary skill in the art at the time this invention was made as evident by the fact that Rosenberg et al uses various percentages of the different polymer matrices to prepare the compositions comprising itraconazole (see Rosenberg et al, examples 1-3, in particular) in order to achieve better solubility and enhanced bioavailability of the antifungal drug at the desired treatment location such as oral cavity. In addition, Baert et al explicitly disclose the preparation of solid dispersion compositions (using the same procedure or processes such as extrusion, or spray drying, as claimed in the instant invention) suitable for use in gastro-intestinal fluid (such as orally administered or ingested formulations of itraconazole) using HPMC and a derivative of crosslinked polyvinylpyrrolidone in various ratio (that includes **HPMC and crosprovidone in a ratio of about 80:20**; see Baert et al, page 12, last paragraph and claim 18), thus an artisan of ordinary skill would have had a reasonable expectation of success in optimizing such ratio between two polymer combinations for the same purposes as claimed in the instant invention.

Thus, the invention as whole would have been *prima facie* obvious to a person of ordinary skill in the drug delivery art at the time the claimed invention was made.

2. Claims 1, 2, 4-6 and 9-29 (as currently amended) are rejected under 35 U.S.C. 103(a) as being unpatentable over Baert et al (WO 97/44014; IDS) in view of Matsumoto & Zografi (Pharm. Res., 1999; IDS) and Jung et al (WO 99/33467; IDS).

Claims are generally drawn to a solid dispersion comprising a poorly soluble bioactive compound dispersed in a polymeric matrix that comprises a first polymer that allows a homogeneous or molecular dispersion of the bioactive compound in the polymer matrix (such as a copolymer of vinylpyrrolidone and vinylacetate), and a second polymer that has a dissolution profile associated with the creation of a micro-environment enhancing the dissolution of the bioactive compound in an aqueous environment (such as hydroxyl-propyl methylcellulose or a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters), wherein said first polymer and said second polymer are present in a ratio of about 70:30, or in a ratio of about 70:30 to about 80:20 (see amended claims 1 and 16, in particular).

Baert et al (IDS) teach antifungal compositions in the form of solid dispersions having improved bioavailability in an aqueous environment such as gastric fluid (see Baert et al, abstract, page 12-13, examples 1-5, and claims, in particular), wherein the polymer matrix comprises a polymer having a stabilizing effect on the bioactive compound (such as antifungal drug, itraconazole) in solution (see page 4, 2nd paragraph, in particular), wherein the polymer allowing enhanced dissolution of the bioactive compound in an aqueous environment is hydroxypropyl methylcellulose (see Baert et al, page 12, in particular), wherein the polymer allowing a homogeneous dispersion is crospovidone (a crosslinked polyvinylpyrrolidone, PVP, i.e. a derivative of PVP akin to a copolymer of vinylpyrrolidone and vinylacetate or PVPVA64 as claimed in the instant invention; see Baert et al, page 10, 3rd and last paragraph, in particular), wherein one or more polymer matrices comprise HPMC and crospovidone. The limitations of claims 9, 10, 23 and 24 are explicitly taught by the referenced invention as Baert et al teach solid dispersions comprising polymer matrix that enhance

bioavailability of an orally administered bioactive compound, such as a class II drug (see the disclosure provided by the applicants, page 3, lines 16-18 of the instant specification), itraconazole/saperconazole (see Baert et al, page 10, in particular). The limitations of instant claims 14, 15, 28 and 29 (wherein the solid dispersions according to claim 1 are prepared by extrusion or spray drying processes; product by process claims) are also met by the solid dispersions comprising itraconazole and polymer matrices such as HPMC and crospovidone (see Baert, discussion supra) that provide enhanced bioavailability to the antifungal drug when ingested orally.

However, solid dispersions comprising a poorly soluble bioactive compound dispersed in two different polymer matrices such as a copolymer of vinylpyrrolidone and vinylacetate (or PVPVA64) in combination with HPMC, or in combination with Eudragit E100, as recited in instant claims, are not explicitly disclosed by the referenced invention of Baert et al.

Matsumato & Zografi (IDS) disclose the use of polyvinylpyrrolidone derivatives including a copolymer of vinylpyrrolidone and vinylacetate (or PVP/VA64, akin to the crosslinked polymer, crospovidone used by Baert et al, i.e. a functional equivalent) in the preparation of solid dispersions of indomethacin (a poorly soluble drug in aqueous solutions; see Matsumato & Zografi, page 1722, materials & methods, and conclusions, page 1728, in particular) in order to enhance the solubility and bioavailability of the drug.

Jung et al (IDS) teach method and composition (solid dispersions) of an oral preparation of itraconazole comprising aminoalkyl methacrylate copolymer (i.e. Eudragit E; see abstract, examples 1-7, tables 3-5, and claims, in particular) that is suitable for

oral ingestion and antifungal treatment. Jung et al also suggest the use of other polymer matrices in combination with Eudragit, such as crospovidone (as diluent; see Jung et al, page 8, 3rd paragraph, in particular).

It would have been obvious to a person of ordinary skill in the art at the time this invention was made to modify the composition taught by Baert et al (i.e. solid dispersions comprising itraconazole comprising two different polymer matrices such as crospovidone and HPMC) such that it comprises of a polymer such as a copolymer of vinylpyrrolidone and vinylacetate (or PVPVA64) as taught by Matsumoto & Zografi, and such that it comprises of a cationic polymer based on dimethylaminoethyl methacrylate and neutral methacrylic esters (such as Eudragit E) as explicitly taught by Jung et al for the preparation of compositions suitable for oral administration and for enhancing the bioavailability in the aqueous environment such as gastro-intestinal tract.

One of ordinary skill in the art would have been motivated at the time of invention to make this kind of modification (i.e. substitution in the polymer matrices, and combinations thereof) in order to obtain suitable solid dispersions with enhanced bioavailability in aqueous environments such as gastric juice or intestinal environment as suggested by the references with a reasonable expectation of success. Since, all the components of composition (i.e. solid dispersions made by extrusion or spray drying processes) as claimed are taught by the referenced inventions of Baert et al (in combination with the disclosures from Matsumoto & Zografi and Jung et al), the claimed subject matter fails to patentably distinguish over the state of the art as represented by

the cited references. Therefore, the instant claims are properly rejected under 35 U.S.C. § 103(a).

The limitation "wherein said first polymer and said second polymer are present in a ratio of **about 70:30 to about 80:20** (or in a ratio of about 70:30, as recited in newly added claim 16), would have been a matter of routine optimization to a person of ordinary skill in the art at the time this invention was made as evident by the fact that Rosenberg et al uses various percentages of the different polymer matrices to prepare the compositions comprising itraconazole (see Rosenberg et al, examples 1-3, in particular) in order to achieve better solubility and enhanced bioavailability of the antifungal drug at the desired treatment location such as oral cavity. In addition, Baert et al explicitly disclose the preparation of solid dispersion compositions (using the same procedure or processes such as extrusion, or spray drying, as claimed in the instant invention) suitable for use in gastro-intestinal fluid (such as orally administered or ingested formulations of itraconazole) using HPMC and a derivative of crosslinked polyvinylpyrrolidone in various ratio (**that includes HPMC and crosprovidone in a ratio of about 80:20**; see Baert et al, page 12, last paragraph and claim 18), thus an artisan of ordinary skill would have had a reasonable expectation of success in optimizing such ratio between two polymer combinations for the same purposes as claimed in the instant invention.

Thus, the invention as whole would have been *prima facie* obvious to a person of ordinary skill in the drug delivery art at the time the claimed invention was made.

*"[E]ven though **product-by-process claims** are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).*

*As per MPEP 2144.06, In order to rely on equivalence as a rationale supporting an obviousness rejection, the **equivalency must be recognized in the prior art**, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958).*

*As per MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be **useful for the same purpose**, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).*

As per MPEP 2144.05 [R3], II. OPTIMIZATION OF RANGES - A. Optimization Within Prior Art Conditions or Through Routine Experimentation: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

*As per PPEP 2144.05 (R-3): In the case where the claimed ranges "**overlap or lie inside ranges** disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are **close enough** that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). "[A] prior art reference that discloses a range encompassing a **somewhat narrower claimed range** is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003).*

Response to Applicant's Arguments

Applicant's arguments with respect to claims 1,2, 4-6, 9-15 (as they pertain to the prior art rejections of record) have been fully considered but are not found persuasive for the following reasons of record.

Applicant's argument (see response, page 7, in particular) that "there is no evidence of record demonstrating a recognition that the percentage of polymer matrix incorporated into composition is a result-effective variable. M.P.E.P. 2144.05(II)(B) ("[a] particular parameter must first be recognized as a result-effective variable" before the determination of optimum or workable ranges of the variable may be characterized as

routine experimentation) (quoting *In re Antonie*, 559 F.2d 618 (CCPA 1977))" is fully considered but is not found to be persuasive. Since, all the components (i.e. solid dispersion comprising a poorly soluble compound comprising polymers) of the claimed composition are well known and are disclosed in the cited prior art relied upon in the obviousness rejections of record (see discussion supra; Rosenberg et al in view of Baert et al or Jung et al; or Baert et al in view of Matsumoto & Zografi and Jung et al), and since, the ratio of polymeric components (or functional equivalents thereof) have explicitly been disclosed (see for example, Baert et al, page 12, last paragraph; Rosenberg et al, page 7, examples 1-3) for attaining the same purpose of optimizing dissolution of a poorly soluble drug (such as itraconazole, which is also exemplified by the applicants; see instant disclosure, figures 12 and 13), the argument of the counsel that "there is no evidence of record demonstrating a recognition that the percentage of polymer matrix incorporated into composition is a result-effective variable" is not found to be persuasive, especially when the claimed invention is recites a polymer ratio of "**about** 70:30".

The argument (see response, page 8, 1st paragraph, in particular) that the prior art reference of Rosenberg et al does not suggest or disclose "varying the ratio of the tow types of polymers" is not found to be persuasive because given the disclosures of the cited prior art references (especially Rosenberg et al, Baert et al, and Jung et al), the use of various proportions of polymers (as exemplified in example 3 of Rosenberg et al) would have been obvious to an artisan of ordinary skill in the drug delivery art at the time the claimed invention was made.

Applicant's arguments (see response, page 8, 2nd paragraph, in particular) regarding the evidence of surprising results (as exemplified in figures 12 and 13 of the instant application) for the combination of two polymers used in the invention to solubilize itraconazole, is interesting. However, the invention as claimed is not commensurate with the evidentiary data provided in the instant specification. The demonstration of unexpected results as presented and argued by applicants are only relevant for the combination of polymers as recited in claims 4 and 6, and not for the broader claims 1 and 16 as presented by applicants. In addition, the data representing the "evidence for surprising results" is commensurated only with a combination of the two polymers in a ratio of 70:30 and 80:20, and not in a ratio of "**about** 70:30 to **about** 80:20" or "**about** 70:30" as presented in claims 1 and 16 (see 112-first rejection of record, above).

Since, the concept of using two different polymers (or functional equivalents thereof) to prepare a solid dispersion composition comprising a poorly soluble drug (or a bioactive compound such as itraconazole) is clearly suggested and disclosed in the cited prior art (see Baert et al, claim 1 and 6, in particular), the obviousness rejection of record is deemed proper.

Conclusion

NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyendra K. Singh whose telephone number is 571-272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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